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REMARKS

Claims 2-16, 21 and 46-49 were pending in this application.

By this Amendment, Applicants have amended claims 2-3, 7-8, 11, 21 and 48-49. These claims are amended based either on the suggestion of the Examiner to whom this application has been assigned or to further clarify the claimed inventions. All of the amended claims are well supported by the specification. Applicants have added new claims 54-64. Applicants maintain that the newly added claims are well supported by the specification.

Correction of Formal Matters

Pursuant to the Examiner's suggestion, Applicants have filed a communication, addressed to the Office of Initial Patent Examination, on February 1, 2006 to update the first paragraph of the specification.

Claim rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 2-16, 21 and 46-49 under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to which it pertains, or with which it is mostly nearly connected, to make and/or used the invention. See page 4 of the October 17, 2005 Office Action.

In response, Applicants respectfully traverse the Examiner's above ground of rejection. Applicants have developed a novel composition and method for reducing the ATP of tumor cells to cytotoxic or cell-killing levels, which is 15% or less of normal ATP level. The specification further disclosed a regimen for selecting suitable

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ATP depleting agents that act synergistically to deplete the cellular ATP levels of tumor cells to below viability. The composition of the present invention uses ATP depleting agents (the selections of which are based on review of literature or experimentation) that work collectively to disrupt the various ATP production pathways of a particular type of tumor cells (such as breast, ovarian, and pancreatic tumor cells).

In the Experimental Details section of the specification (beginning on page 17), which is provided for purposes of illustrating the specific embodiments of the invention and is not intended to limit the scope of the invention, specific combinations of ATP-depleting agents effective in reducing the ATP level of certain tumor cells to 15% or less of normal are discussed. Applicants therefore maintains that a person of ordinary skill in the art following the teaching of the application and the specific examples will be able to prepare a suitable composition based on factors such as tumor cell type, drug resistance characteristics and the involvement of ATP-producing metabolic pathways.

Accordingly, Applicants respectfully request the Examiner to withdraw the above ground of rejection.

Applicants also maintain that new claims 54-64 do not contain the above-mentioned issues.

Claim rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 2-16, 21 and 46-49 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. See page 4 of the October 17, 2005 Office Action.

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In response but without conceding the correctness of the Examiner's position and to expedite the prosecution of this Application, Applicants have added or amended the claims in this application (based on the Examiner's suggestions). Therefore, the claims currently pending in this application do not contain the above-mentioned issues, thereby rendering the above rejection moot.

Non-statutory double patenting rejection

The Examiner rejected claims 2-16, 21 and 46-49 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 20, 22 and 35-47 of copending Application No. 10/172,346. See page 7 of October 17, 2005 Office Action.

In response but without conceding the correctness of the Examiner's position, Applicants will gladly furnish the Examiner with the required terminal disclaimer (if needed) when this application is in condition for allowance except for the terminal disclaimer.

Claim rejections under 35 U.S.C. § 102(b)

1. Nord et al.

Examiner rejected claims 2-3, 5-9, 21 and 46-49 under 35 U.S.C. § 102 as being anticipated by Nord et al. (i.e., page 380, Table 3 (explanation at the top of the table) and associated explanatory text). See page 8 of October 17, 2005 Office Action.

In response, Applicants respectfully traverse the above ground of rejection. Applicants maintain that Table 3 does not disclose that "after 24 hours the ATP level is 10% of

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the normal ATP level", as asserted by the Examiner. The third column of Table 3 indicates the ATP level by percent of control which corresponds to *percent depletion of ATP*. If Table 3 had actually shown that after 24 hours the ATP level is 10% of the normal ATP level, then the value would have been *10% of control (which corresponds to 90% depletion of ATP) instead of the 90% (of control) as shown*. Applicants respectfully direct the Examiner's attention to page 382, right column, 17 lines from the bottom, of Nord et al., wherein 60% of control is stated to be equivalent to a 40% depletion of ATP, and which supports Applicants' interpretation of the data presented in Table 3. Accordingly, Nord et al. cannot anticipate Applicants' claimed invention, and Applicants respectfully request the Examiner to withdraw this ground of rejection.

2. **Stolfi et al.**

Examiner rejected claims 2-3, 5-9, 21 and 46-49 under 35 U.S.C. § 102 as being anticipated by Stolfi et al. (i.e., fourth paragraph of column 1 at page 4075 and the preceding two paragraphs). See page 8 of October 17, 2005 Office Action.

The Examiner further states that "for equivalent references see Colifiori et al. ... at page 1943, paragraph bridging columns 1 and 2; Martin et al. ... in the paragraph bridging pages 656 and 657; and Koutcher et al. ... at page 1145, last two paragraphs of the abstract." See page 8 of October 17, 2005 Office Action.

In response, Applicants respectfully traverse the Examiner's above ground of rejection. According to MPEP § 2131, "[a] claim is anticipated only if *each and every element* as set forth in the claim is found.. in a single prior art reference."

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Claim 2 of this invention recites:

A pharmaceutical composition comprising a pharmaceutically effective amount of ATP-depleting agents in combination with a pharmaceutically acceptable carrier, wherein the ATP-depleting agents synergistically deplete ATP level of cancer cells to 15% or less of normal, and wherein at least one of the ATP-depleting agents is a mitochondrial ATP-inhibitor, a glycolytic inhibitor, a methylthioadenosine phosphorylase inhibitor or an inhibitor of de novo purine synthesis with the proviso that 6-methylmercaptopurine riboside is not one of said inhibitors.

The dependent claims further characterize the combinations of ATP-depleting agents, such as MMPR, 6-AN, PALA, and AL, which are effective in reducing cancer cell ATP to cytotoxic levels, i.e., 15% of normal or below 15% of normal.

Further, Applicants have discovered that the threshold ATP level for achieving tumor regression is 15% of normal ATP level and less, and Applicants have designed and disclosed the combinations of ATP-depleting agents effective for reducing the ATP of cancer cells to cytotoxic levels.

Therefore, since the pending claims do not recite "close to 15% of normal", and since Stolfi et al. only disclose 20% of the normal ATP level, Stolfi et al. cannot anticipate Applicants' claimed invention. Accordingly, Applicants respectfully request the Examiner to withdraw this ground of rejection.

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3. Colifiori et al.

Applicants respectfully traverse the Examiner's above ground of rejection. Applicants maintain that Colofiore et al. do not teach that 15% ATP depletion or greater is a critical level for tumor cell death. Colofiore et al. discuss whether ATP depletion is the cause of cell death or the result of cell death.

See page 1946, last sentence, of Colofiore et al. which states:

"Thus, if there is a possible relationship between ATP depletion and cell death ... Then the combination of these agents (PMA+ADR) might be expected to enhance both ATP depletion and the rate of tumor regressions; those indeed are the findings and support, but do not necessarily constitute, a cause-and-effect relationship."

See also page 1947, left column, second paragraph, which states:

"...it is not clear whether the decrease in ATP is a cause for the dead cells or a result of biochemical analysis of mostly dead cells."

See P. 1947 left column last sentence, bridging to the top of the right column:

"Our newer findings demonstrate that ATP depletion occurred prior to the onset of apoptosis. Thus, it is more likely that ATP depletion is causal to the apoptotic cascade. However, we do not believe that this finding conclusively demonstrates this point, as a still more *direct* causative relationship to apoptosis needs to be documented."

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Applicants respectfully maintain that while Colofiori et al. present data showing the achievement of ATP levels of 19% and 15% of saline control, this reference in no way teaches that depletion of the ATP level to 15% of normal or below 15% of normal is critical to killing cancer cells, particularly in the absence of a conclusive finding of a causal relationship between ATP depletion and cancer cell death. Therefore, a person of ordinary skill in the art would not be motivated to deplete the ATP level of cancer cells to 15% of normal or below 15% of normal to achieve cancer regression.

4. Martin et al.

Upon reviewing the paragraph identified by the Examiner, Applicants did not find any information which would anticipate Applicants' claimed invention. Clarification regarding the relevance of Martin et al. is respectfully requested.

5. Koutcher et al.

Nothing in the Koutcher et al., discloses 15% of normal is critical to killing cancer cells and therefore Koutcher et al. cannot anticipate the claimed invention.

If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

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No fee other than the FIVE HUNDRED AND TEN DOLLARS (\$510.00) for the payment of the three-month extension fee and the FOUR HUNDRED AND SEVENTY FIVE DOLLARS (\$475.00) for the addition claim fee is deemed necessary in connection with the filing of this Communication. However, if any additional fee is required, authorization is given to charge the amount of any such fee to Deposit Account No. 50-1891.

Respectfully submitted,

Albert Wai Kit Chan

I hereby certify that this Amendment is being deposited this date with the U.S. Postal Service with sufficient postage for first class mail addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

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4/17/06

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